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EXAMINER	
LEFFERS JR, GERALD G	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 05/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/430,590	POULTER ET AL.	
	Examiner	Art Unit	
	Gerald G Leffers Jr., PhD	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7,8,10-17,19-32 and 35-51* is/are pending in the application.

4a) Of the above claim(s) *5,7,8,10,11,14-17,22-32,35,36 and 51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,12,13,19-21 and 37-50* is/are rejected.

7)☒ Claim(s) *5,10,11,14,17,35 and 36* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of an amendment, filed 3/4/2004, in which several claims were amended (claims 1, 5, 10-14, 17, 19, 21, 35-36), several claims were cancelled (claims 6, 9, 18) and in which new claim 51 was added. Claims 1-5, 7-8, 10-17, 19-32, 35-51 are pending, with claims 7-8, 15-16 and 22-32 withdrawn from consideration as being directed to nonelected inventions. Claims 5, 10-11, 14, 17, 35-36 and 51 are also withdrawn from consideration as being improperly multiply dependent claims for reasons that are outlined below.

Any rejection of record in the previous office action not addressed herein is withdrawn. This action is FINAL.

Drawings

Receipt is acknowledged of formal drawings filed 3/4/2004. The examiner has not been able to determine whether the drawings submitted on 3/4/2004 comprised color drawings or not due to the new electronic filing system. It would be appreciated if applicants could state in the response to this action whether any of the drawings submitted on 3/4/2004 comprised color figures or photographs. Applicants are reminded of the objections to the drawings raised in the previous office action and are hereby notified that such objections remain if any of the drawings filed on 3/4/2004 comprise color elements. Remedial action as indicated in the last office action is still required in the event that any of the figures filed on 3/4/2004 comprise color elements.

Claim Objections

Claims 10-11, 14, 17, 35-36 and 51 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot be dependent upon another multiply dependent claim. See MPEP § 608.01(n). Accordingly, claims 10-11, 14, 17, 35-36 and 51 have not been further treated on the merits.

Claim 5 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot be dependent upon subsequent claims. See MPEP § 608.01(m)-(n). In addition, MPEP 608.01(m) states:

> **35 U.S.C. 112 indicates that the limitations or elements of each claim incorporated by reference into a multiple dependent claim must be considered separately. Thus, a multiple dependent claim, as such, does not contain all the limitations of all the alternative claims to which it refers, but rather contains in any one embodiment only those limitations of the particular claim referred to for the embodiment under consideration. Hence, a multiple dependent claim must be considered in the same manner as a plurality of single dependent claims.**

If claim 5 is considered as a plurality of single dependent claims, then applicant has improperly claimed the exact same invention in multiple claims (i.e. the retrotransposon consisting of SEQ ID NO: 3). Accordingly, claim 5 has not been further treated on the merits. It would be remedial to amend claim 5 to recite "An isolated retrotransposon consisting of SEQ ID NO: 3."

Claim Rejections - 35 USC § 112 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 12-13, 19-21, and 37-50 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection necessitated by applicants' amendment of the claims in the response filed 3/4/2004.**

Amended claim 12 and dependent claims are directed to an isolated and purified retrotransposon comprising a nucleotide sequence that has at least 95% similarity to (i) SEQ ID NO: 3, (ii) the LTR and POL region of SEQ ID NO: 3 or (iii) to a nucleotide sequence that hybridizes under "stringent" conditions to SEQ ID NO: 3. For each case, the claims read on functional retrotransposable elements. The genus encompassed is a broad one that encompasses a large number of alterations within the sequence described by SEQ ID NO: 3 that allow the resulting nucleic acid to retain function as a retrotransposon. In particular, the limitation of (iii) is egregious in that the recited percent identity is merely to a nucleic acid that hybridizes under undefined "stringent" hybridization conditions to SEQ ID NO: 3, and thus encompasses a much broader genus of nucleic acids than (i) or (ii) that must meet the functional limitation of being a retrotransposon.

Many of the rejected claims comprise the limitation of a "...nucleotide sequence with at least 65% (or 70%, 75%, 80%, 85%, 90%, 95% or 97%) similarity with the LTR and POL region SEQ ID NO: 3...". The rejected claims read on literally any retrotransposon or nucleic acid fragment that comprises a sequence with the recited % similarity to SEQ ID NO: 3. This is an incredibly broad genus of retrotransposons and an even larger genus of nucleic acid fragments.

The instant specification provides no basis for envisioning a representative number of embodiments of, for example, retrotransposons that are only similar at a 65% level with only part of the transposon sequence. The instant specification provides no basis for one of skill in the art to envision nucleic acid fragments that are only 65%-97% similar to the LTR and POL regions of SEQ ID NO: 3 and which retain any sort of retrotransposon activity. Similarly, the specification provides no basis for one to envision embodiments of the claims nucleic acid fragments that retain any of the asserted utilities for the nucleic acid fragments of the invention (e.g. as specific probes for pCal and/or *Candida* species). As pCal appears to be novel in the art, the prior art does not offset the deficiencies of the instant specification with regard to providing a basis for envisioning a sufficient number of specific embodiments as to describe the broadly claimed genus. Therefore, one of skill in the art would have reasonably concluded applicants were not in possession of the claimed invention.

Claim 19, part (a), is further directed to "...a nucleic acid sequence positioned between at least two terminal repeats of the sequence of pCal as described in GenBank accession number AF007776...". Claim 19, part (c), recites a nucleic acid sequence that hybridizes under "stringent" hybridization conditions to the nucleic acid sequence of part (a). The metes and bounds of part (a) are unclear and can be interpreted to encompass literally any nucleic acid sequence sandwiched between the LTR sequences of pCal. The metes and bounds of what constitutes "stringent" hybridization conditions are unclear and undefined in the instant specification, allowing the skilled artisan to read the rejected claims as encompassing almost any hybridization conditions. For these reasons, there is no basis for the skilled artisan to envision a representative number of embodiments of such nucleic acid sequences. Therefore, the skilled

artisan would reasonably have concluded applicants were not in possession of the claimed invention.

Response to Arguments/Written Description

Applicant's arguments filed on 3/4/2004 to similar grounds of rejection made in the previous office action have been fully considered but they are not persuasive. The response essentially argues: 1) the invention involves the retrotransposon of SEQ ID NO: 3, 2) the retrotransposon of SEQ ID NO: 3 is well described in the instant specification (e.g. Examples 2-3 and Figure 2B, 3) the genus claimed with regard to % sequence similarity or stringent hybridization is not overly broad, 4) stringent hybridization conditions were known in the art, and 5) the skilled artisan could envision the claimed embodiments and would face no undue experimentation in determining whether a particular retrotransposon has the claimed structure (i.e. 95% identical to or hybridizing under stringent conditions to SEQ ID NO: 3.

While it is true that many of the embodiments are directed to SEQ ID NO: 3, the rejected claims encompass far more than a small genus of structural/functional variants of SEQ ID NO: 3. For example, and as indicated above, the limitation of part (iii) of claim 12 is particularly egregious in that the recited percent identity is merely to a nucleic acid that hybridizes under undefined "stringent" hybridization conditions to SEQ ID NO: 3, and thus encompasses a much broader genus of nucleic acids than (i) or (ii) that must meet the functional limitation of being a retrotransposon. Possibly more egregious still are the limitations recited in claim 19, parts (a) and (b). For example, claim 19(a) can be read to include *any* sequence inserted between the two terminal repeats of pCal obtained from *any* source. Claim 19, part (c), recites a nucleic acid sequence that hybridizes under "stringent" hybridization conditions to the nucleic acid sequence

of part (a). Thus, claim 19 and dependent claims read on literally *any* nucleotide sequence obtained from *any* source.

As indicated previously, arguments directed to what was conventional in the art at the time of filing concerning "stringent" hybridization conditions are not persuasive because the exact metes and bounds of the term "stringent hybridization" were not art accepted at the time of filing and the specification does not provide an explicit definition of what is encompassed by the term (e.g. see the rejection under 112 2nd paragraph below). Any arguments dependent upon what was art recognized concerning "stringent hybridization conditions" are thus moot.

Arguments directed to the amount of experimentation required to identify those embodiments that meet the functional limitations of the claims are also moot as such arguments are better suited to an enablement rejection and are not persuasive with regard to providing a structural/functional basis for the skilled artisan to envision a sufficient number of specific embodiments to describe the claimed genus of retrotransposons and isolated nucleic acid fragments.

As the instant specification has provided little or no guidance with regard to what changes can be made to the nucleotide sequence described by SEQ ID NO: 3 such that the nucleic acid comprising the changes retains functional activity, there remains no basis for the skilled artisan to envision specific embodiments of the claimed invention such that the broadly claimed genus is described. For these reasons, description of SEQ ID NO: 3 alone is not sufficient to describe the broadly claimed genus of retrotransposons and/or DNA fragments encompassed by the rejected claims.

Claims 1-4 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. ***These grounds of rejection are maintained for reasons of record and repeated. A response to applicants' arguments follows the rejection.***

Although claims 1-4 have already been rejected for lack of written description with regard to retrotransposons encompassed by the limitations recited in claim 12, these claims possess further functional language with regard to the number of "free copies" per cell that necessitate following grounds of rejection.

Claims 1-4 are each drawn towards an isolated retrotransposon having a copy number of "between 40-150 or 50-100 copies" of itself per genome. The retrotransposon can be "free" or episomal, or the retrotransposon can be integrated. The retrotransposon can be isolated from fungi or yeast, or more specifically from *Candida albicans*. The broadest embodiments potentially encompass literally any eukaryotic cell type that might harbor a retro-transposable element (e.g. corn, yeast, human, fly, etc.). Even in more specific embodiments, the claims encompass any strain of *Candida* or, more specifically, *Candida albicans*. Each of the claims comprises the functional limitation of between 40 and 150 copies of itself per host cell genome.

The specification teaches one embodiment of the claimed invention (pCal or Tca2) which is found at high copy number in a few particular strains of *C. albicans*. No definitive explanation is provided in the specification for why pCal is maintained at such high copy number in these particular strains of *C. albicans* and not in others. For example, the mechanism could

involve some mutation in pCal or a mutation in the particular host, or a combination of mutations in both the host and pCal. The prior art is of no help in describing a mechanistic rational for maintenance of such high copy numbers because the art does not appear to teach such numbers.

Given the large number of host cell types and retrotransposable elements potentially embraced by the rejected claims and the presence of the functional limitation for high copy number, the presence of only a single relevant example in the specification or prior art meeting the functional limitation for high copy number and the lack of teachings from the specification or prior art as to how such a high copy number is attained by the single relevant example, one of skill in the art would not be able to envision a representative number of specific embodiments of the claimed invention to describe the potentially broad genus of such retrotransposable elements embraced by the rejected claims. Therefore, one of skill in the art would reasonably conclude applicants were not in possession of the claimed invention at the time of filing.

Response to Arguments/Written Description-"Free copies"

Applicant's arguments filed on 3/4/2004 have been fully considered but they are not persuasive. Claim 1 has been amended to recite that the isolated and purified retrotransposon maintains 40-150 free copies of itself per cell in *Candida albicans*. The response essentially argues: 1) the invention involves the retrotransposon of SEQ ID NO: 3, 2) the retrotransposon of SEQ ID NO: 3 is well described in the instant specification (e.g. Examples 2-3 and Figure 2B, 3) the genus claimed with regard to % sequence similarity or stringent hybridization is not overly broad, 4) stringent hybridization conditions were known in the art, and 5) the skilled artisan could envision the claimed embodiments and would face no undue experimentation in

determining whether a particular retrotransposon has the claimed structure (i.e. 95% identical to or hybridizing under stringent conditions to SEQ ID NO: 3.

The amendment of the claims to increase the % similarity required to satisfy the claim limitations of claim 12, upon which claims 1-4 depend is appreciated and does narrow the genus of retrotransposons encompassed by the rejected claims to some degree. Likewise, the amendment of the rejected claims to recite that the retrotransposon maintains the free copies of itself in a Candida albicans host cell also narrows the genus to some degree. However, for several reasons these changes are not sufficient to overcome the grounds of rejection given above. For example, it is noted that the % similarity is to a nucleotide sequence that hybridizes under undefined "stringent" conditions to SEQ ID NO: 3 and not directly to the retrotransposon of SEQ ID NO: 3 itself. Thus, claim 12 still encompasses embodiments where the % similarity is to a broad genus of nucleic acid sequences rather than to the defined sequence described by SEQ ID NO: 3. Further, and as pointed out previously, applicants' assertion that the metes and bounds of what constitutes "stringent" hybridization were clear in the art at the time of filing are inaccurate and, thus, the rejected claims still encompass a potentially large genus of retrotransposons that must meet the very specific functional limitations of claims 1-4 and 6 regarding the ability to maintain 40-150 free copies in the host cell. There is no description in the prior art or instant specification of those components of the retrotransposon of SEQ ID NO: 3 that enable the retrotransposon consisting of SEQ ID NO: 3 to maintain itself at 40-150 copies per *C. albicans* host cell. Therefore, there is and was no basis for the skilled artisan to predictably envision those embodiments that would necessarily satisfy the functional limitations of the claims. For these reasons, and those recited above, the skilled artisan would reasonably

have concluded applicants were not in possession of the claimed genus of retrotransposons at the time of filing.

Claims 1-4 12-13, 19-21 and 37-50 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for embodiments limited to the retrotransposable element pCal or TCa2 (i.e. as described by SEQ ID NO: 3), or nucleic acid fragments thereof, does not reasonably provide enablement for embodiments wherein the retrotransposable element is other than pCal or TCa2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. **These grounds of rejection are maintained for reasons of record in the office action mailed 12/05/2003 and repeated below.**

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The rejected claims are all directed to a retrotransposable element and/or DNA fragment designated pCal (episomal form) or TCa2 (integrated form) described by SEQ ID NO: 3, or variants thereof retaining the structural/functional characteristics of a retrotransposable element.

Breadth of the claims: The base claims (claims 12 and 19) encompass embodiments that 1) comprise a nucleotide sequence with at least 65% (or 70%, 75%, 80%, 85%, 90%, 95% or

97%) similarity to the LTR and POL regions of SEQ ID NO: 3 (present in deposit AF007776), 2) nucleic acids that hybridize to either SEQ ID NO: 3, or 3) hybridizes under stringent conditions to a nucleic acid sequence sandwiched between at least two of the terminal repeat sequences of the nucleic acid deposited in GenBank as AF007776. The "stringent" hybridization conditions have not been explicitly defined and can be broadly read to encompass almost any hybridization conditions. Thus, the rejected claims encompass an enormously broad genus of retrotransposable elements and/or nucleic acid fragments that must either function as retrotransposable elements (e.g. claim 12) or function in some utility that corresponds to the asserted utilities for pCa1 or TCa2.

Functionally, several of the claims recite the limitation that the retrotransposable element is found as an extrachromosomal DNA molecule having a copy number of 40-150 free DNA copies per cell. This greatly exacerbates the complexity of the claimed invention as it requires at least some understanding as to how pCal maintains such a high copy number of itself in the host cell.

Guidance of the specification/The existence of working examples: The instant specification teaches the isolation and general characteristics of a retrotransposable element from *Candida albicans* termed pCal in its extrachromosomal form and TCa2 in its integrated form. Remarkably, pCa1 is maintained at ~40-150 "free" copies of itself per cell, as well as in an integrated form. The specification teaches that portions of pCa1 can be used as probes to identify pCa1 or TCa2, and/or to identify strains of Candida comprising the retrotransposable element.

The specification does not teach, however, what portions of SEQ ID NO: 3 are required for retrotransposon activity, much less what portions are required for maintaining 40-150 episomal copies per cell.

State of the art/Predictability of the art: The retrotransposable element described by SEQ ID NO: 3 (pCa1 or TCa2) appears to have been novel in the art at the time of filing. It appears to have been novel in the art as well with regard to its ability to maintain such high copy numbers of itself in the host cell in a stable, episomal manner. Therefore, the prior cannot offset the deficiencies of the instant specification with regard to those elements of SEQ ID NO: 3 required for functional activity.

Given the broad genus of retrotransposable elements and nucleic acid fragments encompassed by the rejected claims, and given the lack of significant teachings in the prior art concerning the functional/structural characteristics of SEQ ID NO: 3, making and using the claimed invention in the broad scope encompassed by the rejected claims would necessarily have been unpredictable, requiring trial-and-error experimentation.

The amount of experimentation necessary: Given the combination of the factors outlined above, it would have required undue, unpredictable experimentation in order to make and use the invention commensurate in scope with the rejected claims. For example, for embodiments wherein the nucleic acid is required to retain retrotransposon activity, one would have had to first envision possible changes to the sequence described by SEQ ID NO: 3 (~6 kb in length) that might retain functional activity, construct nucleic acids comprising the activity, and test such recombinant constructs to determine that the resulting structure retained the ability to function as a retrotransposon in a given host cell. Alternatively, for embodiments where the nucleic acid is

used to probe for the presence of SEQ ID NO: 3 in a host cell, one would have first had to envision changes to SEQ ID NO: 3 that would allow the resulting nucleic acid to retain the ability to bind to SEQ ID NO: 3 in a specific manner, construct such nucleic acid fragments, and then test the fragments to see if the recombinant nucleic acids retain the ability to bind to SEQ ID NO: 3 in a specific manner such that the nucleic acid could be used a probe for a host strain comprising pCal or TCa2. In either case, the experimentation required would have to have been trial-and-error in nature and would necessarily have been undue given the combination of the factors outlined above. Therefore, the instant specification is found to be enabling only for those embodiments directed to SEQ ID NO: 3 or fragments thereof.

Response to Arguments/Enablement

Applicant's arguments filed on 3/4/2004 have been fully considered but they are not persuasive. Claim 1 has been amended to recite that the isolated and purified retrotransposon maintains 40-150 free copies of itself per cell in *Candida albicans*. The response essentially argues: 1) the invention involves the retrotransposon of SEQ ID NO: 3, 2) the retrotransposon of SEQ ID NO: 3 is well described in the instant specification (e.g. Examples 2-3 and Figure 2B, 3) the genus claimed with regard to % sequence similarity or stringent hybridization is not overly broad, 4) stringent hybridization conditions were known in the art, and 5) the skilled artisan could envision the claimed embodiments and would face no undue experimentation in determining whether a particular retrotransposon has the claimed structure (i.e. 95% identical to or hybridizing under stringent conditions to SEQ ID NO: 3.

These arguments have been dealt with above with regard to the written description rejections and the counterarguments presented by the examiner above are incorporated here as

well. As indicated above, the rejected claims are not limited to a relatively narrow genus of retrotransposons and/or nucleic acid sequences comprising SEQ ID NO: 3, or fragments thereof. The genus of potential retrotransposons and/or nucleic acid sequences encompassed by the claims is far larger and embraces a very large number of sequences that would not be expected to function as a retrotransposon or which could not readily be used, for example, to identify pCal or TCa2 in a sample. While assays may exist to identify the functional embodiments of the claimed retrotransposons and/or nucleic acid sequences, these assays are merely assays for screening and do no provide a predictable basis for production of the claimed elements that meet the functional requirements of the claims. The skilled artisan is therefore dependent upon the prior art for guidance as to how to construct and use those embodiments in a manner that does not require undue experimentation. For the combination of reasons outlined above, it would have taken the skilled artisan undue, unpredictable experimentation of a trial-and-error nature to produce and use the invention commensurate in scope with the broadly claimed genus retrotransposons and/or nucleic acid sequences.

Claim Rejections - 35 USC § 112 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4, 13, 19-21, 37-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 13 is vague and indefinite in that the metes and bounds of the phrase "wherein the isolated and purified retrotransposon is integrated into the genome of a cell" are unclear. It is unclear how the claimed "integrated" form can be isolated and purified, as recited in claim 12, if it is integrated into a host genome. **This rejection is maintained.**

Claim 19 is vague and indefinite in that the metes and bounds of the phrase "...a nucleic acid sequence positioned between at least two terminal repeats of the sequence of pCal as described in GenBank accession number AF007776..." are unclear. **It is unclear whether the claim is limited only to the transposable element found in AF007776 (i.e. pCal), or whether it is also directed to literally *any* nucleic acid sequence sandwiched between the LTR's found within the transposable element found in AF007776.** It would be remedial to amend the claim language to clearly indicate whether part (a) is directed solely to pCal, or encompasses any DNA sequence sandwiched between the LTR's of pCal. **This rejection is maintained.**

Claims 12 and 19 are vague and indefinite in that the metes and bounds of the phrase "...hybridizes under stringent conditions..." are unclear. **This rejection is maintained for reasons of record repeated here.** The phrase is unclear in that the term "stringent hybridization conditions" is not clearly defined in the specification. The concept of what qualifies as "stringent" conditions is likely to vary from investigator to investigator, and is highly subjective. It would be remedial to amend the claim language to explicitly recite the "stringent" hybridization conditions (i.e. salt conditions, temperature, etc.).

Response to Arguments/112 2nd Rejections

Applicant's arguments filed 3/4/2004 have been fully considered but they are not persuasive. The response reiterates its arguments that "stringent" hybridization conditions were

described in the instant specification (e.g. pages 26-28) and that the term is well known and understood in the art. The response asserts that claim 13 has been amended for clarity. The response further argues that claim 19(a) is directed to the sequence of pCal that is located between the terminal repeats, but that this sequence can comprise a nucleic acid encoding any desired protein as the retrotransposon can be used as an expression vector for any heterologous sequence.

Applicants' response with regard to claim 13 does not address the issue of how the isolated and purified retrotransposon can be considered as "isolated and purified" when it is in the context of a host cell genome. It would be remedial to amend the claim to recite a host cell comprising the isolated and purified retrotransposon of claim 12.

With regard to the term "stringent hybridization", as indicated previously, the specification merely cites a couple of prior art references where different hybridization conditions are taught. However, there remains no explicit definition in the specification as to what such conditions necessarily encompass so that the skilled artisan cannot rely on the specification to determine the metes and bounds of the term. Second, the assertion that the term is well known and understood in the art is not supported and implies that a specific set of conditions were art recognized as being "stringent" hybridization conditions. As stated in making the rejection, such "stringent" hybridization conditions are and were likely to vary from investigator to investigator and are, therefore, vague and indefinite unless explicitly defined by the specification.

Applicants assertion that claim 19(a) is directed to the sequence of pCal that is located between the terminal repeats of pCal as well as any sequence that can be positioned between the

terminal repeats of pCal is not supported by the current claim language. The claim can still be read to encompass *any* sequence inserted between the two terminal repeats of pCal as deposited at AF007776 or as being *necessarily* limited to the sequence that is actually deposited. The two possibilities are exclusive. In fact, the claim is further indefinite in that it is directed to an isolated nucleic acid fragment so that it is now unclear as the claim is written as to whether the nucleic acid fragment *necessarily* comprises the two terminal repeats of pCal.

Allowable Subject Matter

Claims limited to SEQ ID NO: 3 and fragments thereof appear to be allowable over the prior art and meet 112 1st requirements. Claim 5 would be allowable if claimed as an independent claim directed to a retrotransposon consisting of SEQ ID NO: 3.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr., PhD whose telephone number is (571) 272-0772. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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